Management of the presumed susceptible varicella (chickenpox)-exposed gravida: a cost-effectiveness/cost-benefit analysis
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The management of the presumed susceptible varicella (chickenpox)-exposed gravida. Three different management strategies of varicella-zoster immune globulin prophylaxis against varicella (chickenpox) infection in exposed gravidas were explored:

A do-nothing or observation strategy;

An immune-testing strategy, in which varicella-zoster immune globulin is administered only if the gravida tests non-immune;

A universal administration strategy, in which varicella-zoster immune globulin is administered to all exposed gravidas with a negative or indeterminate history of infection.

Type of intervention
Screening; primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
A theoretical 25 year-old pregnant woman with a 55-year life expectancy, susceptible to varicella infection.

Setting
This hypothetical study is based on a hospital setting. The economic study was performed in Alabama, USA.

Dates to which data relate
The dates of the data were not explicitly stated. Effectiveness estimates were extracted from studies published in 1986 and 1987, and expanded by the authors' opinions. The resource data were estimated using data from 1962-1981. The cost of varicella-zoster immune globulin was taken from a document dated 1984, and the cost per day of hospitalisation was taken from statistics dated 1993.

Source of effectiveness data
Two uncontrolled investigations were used, supplemented by the authors’ own opinions and judgements.

Modelling
A decision analysis model using Decision Maker was developed to combine estimates of effectiveness and costs of the
three different management strategies.

Methods used to derive estimates of effectiveness
Estimates of effectiveness derived from the literature were adjusted according to the authors’ own opinions and judgements.

Estimates of effectiveness and key assumptions
In two studies of healthy non-pregnant women (aged over 20), the mortality rate for varicella infection was 31/100,000 and the hospitalisation rate was 127/10,000. Two studies in pregnant women, one retrospective and one prospective, reported the mortality rate from varicella as 1/43 and 1/150 respectively. The authors of the cost-effectiveness analysis felt that these were only relevant to the most severe cases. Therefore, the authors used a wide range of estimates. No infection transmission rates existed for varicella in pregnant women. One study demonstrated that 90% with household exposure compared to 18% with casual or transient exposure became infected. For the baseline, the authors selected 90% (household exposure) as the infection transmission rate. For probability of immunity to varicella, six studies reported rates of 72-89%. The authors selected 80% as the baseline immunity rate. The mean sensitivity and specificity of varicella-zoster virus antibody assays were 95% and 84% respectively. Bayes’ theorem was used to calculate the actual probability of immunity for a positive or negative test result, given the assumption of an 80% immunity rate. Two uncontrolled investigations showed varicella-zoster immune globulin to modify the severity or prevent varicella infection if administered within 96 hours of exposure. However, efficacy rates for varicella-zoster immune globulin were not available and so a wide range of potential efficacy from 1 to 99% was evaluated.

Measure of benefits used in the economic analysis
The measures of benefit were life-years gained and resource savings. A decision analysis model using Decision Maker was developed to estimate life years gained by the alternatives.

Direct costs
Quantities and costs were considered separately. Only health service costs were considered: varicella-zoster immune globulin, immunity diagnostic test and hospitalisation costs. The estimation of the cost of varicella-zoster immune globulin was based on the fee charged by the American Red Cross plus a small administration fee, and the immunity diagnostic test was based on the fees charged at the Children’s Hospital of Alabama. The mean length of stay for an adult with varicella was estimated from a published study of patients of Olmsted County, Minnesota (1962), and the cost per day for an acute-care hospitalisation was estimated from American Hospital Association statistics (1993).

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was performed to deal with uncertainty in the variables such as the varicella hospitalisation rates and mortality rates in pregnancy, varicella-zoster immune globulin efficacy, the infection transmission rate, the discount rate for life-years gained, the cost of immunity testing, and the rates and costs of hospitalisation.

Estimated benefits used in the economic analysis
Benefits in terms of life-year gained and resource savings were not explicitly reported.

Cost results
The baseline cost for varicella-zoster immune globulin was $400, immune testing $25, and hospitalisation for 7 days $5,740.
Synthesis of costs and benefits
By varying the mortality rate in the range from 31(1X) to 2,540 (100X) per 100,000 cases at each discount rate of 0%, 5% (baseline) and 10%, efficacies were determined and compared against a $50,000 per life-year threshold to test whether the immune-testing strategy would be cost-effective. For example at a mortality rate of 155/100,000 cases and at a 5% discount rate, the efficacy would have to be 49% for varicella-zoster immune globulin to be cost-effective. However if the mortality rate were decreased to 31/100,000 cases, then varicella-zoster immune globulin would not be cost-effective even with perfect efficacy. The universal strategy was less cost-effective than the testing strategy and it was only acceptable in an incremental analysis at higher mortality and efficacy rates. For example at a mortality rate of 310/100,000 cases and 75% efficacy, the incremental cost-effectiveness of universal administration generated was $233,000 per life-year gained. It was only when the cost of immune testing was increased from $25 to $316, that the universal administration strategy became a more cost-effective alternative to the immunity-testing strategy.

These observations were reflected in terms of resource savings to costs. Resource savings/cost ratios were calculated for the immune-testing strategy by varying potential hospitalisation rates in the range from 127 (1X) to 2540 (20X) per 10,000 cases at efficacy rates of 75% and 95%. For example at a hospitalisation rate of 635/10,000 and at 75% efficacy, the savings/cost ratio of the immune-testing strategy was 0.38. If the baseline cost of maternal hospitalisation were doubled from $5,740 to $11,480, the respective savings/cost ratio would increase to 0.76. However if the baseline cost of hospitalisation was $17,220, the saving/cost ratio would increase to 1.1 and hence the immune-testing strategy would be more cost saving than the universal strategy.

Authors' conclusions
The authors recommend the vigorous use of the immune-testing strategy, except at very high estimates of varicella-zoster immune globulin efficacy and at very high mortality rates. Furthermore the tests of immunity are sensitive, specific and inexpensive, and it is estimated that 72-89% of presumed gravidas are immune. The authors acknowledged that the lack of population-based estimates for rates of severe complications due to varicella infection and the minimal amount of data available for the efficacy of varicella-zoster immune globulin limited their analysis. However the larger question of whether prophylactic measures should be taken, cannot be answered by this study.

CRD COMMENTARY - Selection of comparators
Whilst the choice of comparators was not explicitly justified, they do appear to represent variations of usual practice, and are therefore sensible.

Validity of estimate of measure of benefit
The study was based on estimates from published studies, and adjusted by the authors' opinion and judgement. The baseline estimates may not be accurate, but sensitivity analysis was used adequately to compensate for uncertainty in these variables. Reporting of benefits in terms of life-years gained for each permutation of mortality rate, hospitalisation rate, efficacy and discount rate would have been helpful. In particular the method of determination of the cost-effectiveness ratios used by the authors to compare against the threshold is not immediately obvious and explicit. The analysis only addressed maternal outcomes as there is no evidence that varicella-globulin would prevent viremia, fetal infection, or congenital varicella syndrome.

Validity of estimate of costs
Insufficient details were provided of the source and nature of the costs.

Other issues
The authors used $50,000 per life-year gained as a threshold for cost-effectiveness. This was a rather subjective figure to use. It implies a shadow price for a life-year gained i.e. society's willingness to pay for a life-year. It is unlikely that the shadow price would be independent of the size of the management strategy. Also the management strategy's true opportunity cost can only be assessed by examining what is foregone in other sectors. The authors stated that the study
contains a cost-benefit analysis. For inclusion in this database a study is not regarded as a cost-benefit analysis if the savings of resources are considered as benefits (outcomes). The cost data and the clinical data (i.e. immunity rate) may not be generalisable to other countries.

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